Paper No. 21

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte ALAIN H. ROOK

Appeal No. 2003-1609
Application No. 09/419,328

ON BRIEF

Before WINTERS, WILLIAM F. SMITH, and ADAMS, Administrative Patent Judges.

ADAMS, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on the appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 1, 3, and 4. The claims are reproduced below:

1. A method for treatment of advanced cutaneous T cell lymphoma in a human comprising administering to a human an effective amount of recombinant interleukin-12 in a pharmaceutically acceptable carrier.

3. A composition for treatment of advanced cutaneous T cell lymphoma in a human comprising recombinant interleukin-12 and an adjunct therapeutic agent which stimulates interferon-γ production, said adjunct therapeutic agent comprising a retnoid, interleukin-18, interferon-α or interferon-γ.

4. A method for treatment of advanced cutaneous T cell lymphoma in a human comprising administering to a human an effective amount of recombinant interleukin-12 in a pharmaceutically acceptable carrier

and an adjunct therapeutic agent which stimulates interferon-γ production.

The references relied on by the examiner are:

Rook et al. (Rook '97), "Pathogenesis of cutaneous T-cell lymphoma: implications for the use of recombinant cytokines and photophoresis", Clin. Exp. Immunol., Vol. 107, Supp. 1, pp. 16-20 (1997)

Rook et al. (Rook '96), "The Potential Therapeutic Role of Interleukin-12 in Cutaneous T-Cell Lymphoma," Ann. New York Acad. Sci., Vol. 795, pp. 310-18 (1996)

Verbik et al. (Verbik), "In vivo therapeutic effects of interleukin-12 against highly metastatic residual lymphoma," Clin. Exp. Metastasis, Vol. 14, pp. 219-29 (1996)

GROUNDS OF REJECTION

Claim 1 stands rejected under 35 U.S.C. § 102(b) as being anticipated by Rook '97.

Claims 1 and 3 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over the combination of Rook '96 and Verbik.

Claim 3 stands rejected under 35 U.S.C. § 103(a) as being unpatentable over the combination of Rook '96, Verbik and Rook '97.

Claim 4 stands rejected under 35 U.S.C. § 103(a) as being unpatentable over Rook '96.

We affirm the rejection of claim 1 and 3 over the combination of Rook '96 and Verbik. We reverse the rejection of claim 1 under 35 U.S.C. § 102(b) and claim 4 under 35 U.S.C. § 103(a). Given our disposition, we do not reach the merits of the rejection of claim 3 under 35 U.S.C § 103(a) as being unpatentable over Rook '96, Verbik and Rook '97.

Discussion

The rejection of Claim 1 under 35 U.S.C. § 102(b):

Anticipation requires that the prior art reference disclose, either expressly or under the principles of inherency, every limitation of the claim. In re King, 801 F.2d 1324, 1326, 231 USPQ 136, 138 (Fed. Cir. 1986); RCA Corp. v. Applied Digital Data Sys., Inc., 730 F.2d 1440, 1444, 221 USPQ 385, 388 (Fed. Cir. 1984). But to be prior art under § 102(b), a reference must be enabling. Paperless Accounting, Inc. v. Bay Area Rapid Transit Sys., 804 F.2d 659, 665, 231 USPQ 649, 653 (Fed. Cir. 1986); In re Donohue, 766 F.2d 531, 533, 226 USPQ 619, 621 (Fed. Cir. 1985) (citing In re Sasse, 629 F.2d 675, 681, 207 USPQ 107, 111 (CCPA 1980)). That is, it must put the claimed invention in the hands of one skilled in the art. Donohue, 766 F.2d at 533, 226 USPQ at 621.

According to the examiner (Answer, page 4), Rook '97 "discloses that there is deficient interferon-gamma (IFN-γ) production and a marked defect in IL-12 [(interleukin-12)] production in advanced cutaneous T cell lymphoma [(CTCL)] ... and that in vitro studies demonstrate that IL-12 can correct the deficient IFN-γ production and cell-mediated cytotoxicity...." In this regard, the examiner finds (id.), Rook '97 "teaches that his experimental results led to phase I/II clinical trials of recombinant IL-12 for treatment of CTCL, wherein IL-12 is administered subcutaneously...."[1] In support of this assertion, the examiner relies on Rook '97, page 18, column 1, lines 18-20, wherein the reference states "[a]t the time of

[1] In addition, the examiner asserts (id.), while Rook '97 does not teach the use of a pharmaceutically acceptable carrier "it is well known in the art that a purified protein agent is virtually always used in combination with other agent(s) (such as dissolving solutions) rather than used as its crystal form alone."

this writing, phase I/II trials of recombinant IL-12 administered subcutaneously for CTCL have commenced at our institution."

In response, appellant submitted the Rook Declaration to clarify the meaning of the statement in Rook '97 that phase I/II trials have commenced. Specifically, Rook declares (Declaration, page 2), "[a]lthough clinical trials were reported to be underway, they were only in the planning stages. Being that Phase I trials were still in planning stages, no patients had yet actually participated in the study." In addition, Rook declares (id., bridging paragraph, pages 1-2)

> [I]t was not until after 1997 and the publication of the paper by Rook et al. that it was actually demonstrated that IL-12 was effective against CTCL ... [I]nitial studies administering IL-12 to cancer patients suffereing with malignant melanoma resulted in no clinical response. Hence, IL-12 was not considered to be effective."

Accordingly, appellant asserts (Brief, page 8), Rook '97 "does not anticipate the instant invention of claim 1 which is drawn to treatment of advanced ... [CTCL]. It is only with the specification in hand that describes results of treatment of humans that one of skill would see that the invention of claim 1 had been reduced to practice."

In response the examiner asserts (Answer, page 10), "the Rook ['97] reference is a statutory bar under 35 U.S.C. [§] 102(b) and thus cannot be overcome by an affidavit or declaration under 37 CFR [§] 1.131." We note, however, that nothing on the face of the Declaration suggests that it was filed under 37 CFR § 1.131. We also note that the examiner agrees (Answer, page 12), with appellant's assertion (Brief, page 7) that, "Phase I clinical trials are

merely safety studies.... A Phase I clinical trail is not a study of efficacy of a drug, or the ability of a candidate compound to produce a pharmacological effect that has therapeutic potential." According to appellant's claim 1, an "effective amount" of IL-12 is administered to a human for treatment of advanced CTCL. The examiner has identified no disclosure in Rook '97 of an amount of IL-12 that would be effective to treat advanced CTCL. Instead, the sole basis for the examiner's assertion is a single sentence in Rook '97 that phase I/II trials have commenced. The Rook Declaration, however, clarifies that while the reference states that trials had commenced, they were actually only in the planning stages.

For the foregoing reasons, we disagree with the examiner's statement that Rook '97 "clearly enables one of skill in the art to practice the method because it discloses a specific agent for a specific disease in a specific species (humans) by a specific route of administration." To the contrary, the evidence of record, suggests that there was interest in using IL-12 to treat advanced CTCL, but that this interest was only in the preliminary stages of development.[2] There was no evidence that IL-12 would be effective in the treatment of advanced CTCL, or what amount of IL-12 would be effective to accomplish that goal. Therefore, in our opinion, the Rook '97 reference does not provide an enabling disclosure of the invention set forth in appellant's claim 1.

Accordingly, we reverse the rejection of claim 1 under 35 U.S.C. § 102(b) over Rook '97.

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[2] In this regard, we note that the text immediately preceding the sentence relied upon by the examiner state "it is possible that the administration of IL-12 to patients with CTCl would result in a clinically significant anti-tumour effect. Clinical trials using IL-12 alone and together with other active biological agents is clearly warranted...." Rook '97, page 18, column 1, lines 13-17.

The rejection under 35 U.S.C. § 103(a) over Rook '96 and Verbik:

According to appellant (Brief, page 4), claims 1 and 3 stand or fall together under 35 U.S.C. § 103(a) over the combination of Rook '96 and Verbik. Since claims 1 and 3 stand or fall together, we limit our discussion to representative independent claim 3. Claim 1 will stand or fall together with claim 3. 37 CFR § 1.192(c)(7) (2001).

The composition of claim 3 requires recombinant IL-12 and an adjunct therapeutic agent that stimulates IFN-γ production. According to claim 3, this "adjunct therapeutic agent" can be (1) a retinoid; (2) IL-18, (3) IFN-α or (4) IFN-γ. Therefore, to the extent that appellant relies on the intended use language set forth in the composition of claim 3 (see e.g., Brief, page 11), we note as set forth in In re Zierden 411 F.2d 1325, 1329, 162 USPQ 102, 104 (CCPA 1969):

> A mere statement of a new use for an otherwise old or obvious composition cannot render a claim to the composition patentable. As we said in In re Lemin, 51 CCPA 942, 326 F.2d 437, 140 USPQ 273, 276 (1964),
>
> > Appellants are clearly correct in demanding that the subject matter as a whole must be considered under 35 U.S.C. 103. But in applying the statutory test, the differences over the prior art must be more substantial than a statement of the intended use of an old composition. ... It seems to us that the composition ... would be exactly the same whether the user were told to cure pneumonia in animals with it ... or to promote plant growth with it (as here). The directions on the label will not change the composition....

See also, In re Spada, 911 F.2d 705, 708, 15 USPQ2d 1655, 1657 (Fed. Cir. 1990) ("[t]he discovery of a new property or use of a previously known composition, even when that property and use are unobvious from the prior art, cannot impart patentability to claims to the known composition").

According to the examiner (Answer, page 15), Rook '96 teaches and suggests the limitations of claim 3. In support of this assertion the examiner finds (Answer, bridging paragraph, pages 15-16, emphasis and modification original), Rook '96

> states that "in view of the specific immune defects in association with advanced CTCL, ... the institution of controlled trials using recombinant IL-12 alone and with other Th1-inducing agents should be pursued" (page 316, the third paragraph), and that "retinoid compounds exert beneficial therapeutic effects for CTCL", and "as an adjunct to the use of cytokine therapy for CTCL, our preliminary data indicate that retinoid appear to produces [sic] effects on IFN-γ [Th1 cytokine] production that should beneficially alter the cytokine "imbalance" in CTCL" (page 316, the second paragraph).

Accordingly, we agree with the examiner in that Rook '96 suggests a composition comprising recombinant IL-12[3] and a retinoid. Based on the teachings of Rook '96, it is our opinion that it would have been prima facie obvious to prepare a composition comprising recombinant IL-12 and a retinoid, as suggested by Rook '96 to be used with a reasonable expectation of success in in vitro studies (as described in Rook '96 for each compound individually), leading ultimately to controlled in vivo trials.

"A prima facie case of obviousness is established when the teachings from the prior art itself would appear to have suggested the claimed subject matter to a person of ordinary skill in the art." In re Bell, 991 F.2d 781, 782, 26 USPQ2d 1529, 1531 (Fed. Cir. 1993) (quoting In re Rinehart, 531 F.2d 1048, 1051, 189 USPQ 143, 147 (CCPA 1976)). In our opinion, the examiner has met her burden of providing the evidence necessary to establish a prima facie case of

[3] Regarding "recombinant IL-12," we note that Rook '96 used recombinant IL-12 in their studies. See e.g., Rook '96, bridging paragraph, pages 312-313.

obviousness. Accordingly, the burden of coming forward with evidence or argument was properly shifted to the appellant. In re Oetiker, 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992).

On this record, the majority of appellant's arguments are directed at Verbik. Regarding Rook '96, appellant's arguments are limited to what appellant characterizes as the failure of Rook '96 to teach "a method of in vivo [sic] treatment using IL-12" or the "administration of IL-12 even in vitro with an adjunct therapeutic agent as claimed in claim 3." See e.g., Brief, page 11; see also Reply Brief, page 5 ("[t]he Examiner acknowledges that Rook et al. (1996) do not teach a method of in vivo treatment."). We note, however, that for claim 3, the examiner has based her conclusion of obviousness solely on Rook '96. See e.g., Answer, bridging paragraph, pages 6-7, and first full paragraph, page 7. We find no error in the examiner's rejection. In re Kronig, 539 F.2d 1300, 1302-03, 190 USPQ 425, 426-427 (CCPA 1976).

Regarding Verbik, we note appellant's assertion (Brief, bridging paragraph, pages 11-12), that Verbik teach "that early deaths resulted with use of IL-12 in animals, not just a minor toxic effect but a life-threatening one, indicates that the use of IL-12 in conjunction with other therapeutics especially needs to be shown to be safe before testing in humans is begun." To the extent that appellant is arguing that Verbik teaches away from the claimed invention, we disagree. As the examiner explains (Answer, page 14),

> [t]he unexplained early death in the test mice was not a consequence of IL-12 treatment, rather, it was resulted from a combination treatment of IL-12 and IL-2-ASC. ... Similarly, the severe gastrointestinal damage in the experimental animals

> observed by others and cited by Verbik was a result of a combination of lethal radiation with IL-12...It is the appellant's assertion, not Verbik's belief, that it was IL-12 was [sic] leading to unacceptable toxicity.... Contrary to the appellant's assertion, Verbik demonstrates clearly that IL-12 alone exhibits [a] strong in vivo antitumor effect ... and no early death for IL-12 treated mice comparing [sic] to mice in the control group....

For the foregoing reasons, we find no error in the examiner's rejection. Accordingly, we affirm the rejection of claim 3 under 35 U.S.C. § 103(a) as being unpatentable over the combination of Rook '96 and Verbik. As set forth above, claim 1 falls together with claim 3.

The rejection under 35 U.S.C. § 103(a) over Rook '96, Verbik and Rook '97:

Having affirmed the rejection of claim 3 under 35 U.S.C. § 103(a) as being unpatentable over the combination of Rook '96 and Verbik, we do not reach the merits of the rejection of claim 3 under 35 U.S.C. § 103(a) as being unpatentable over the combination of Rook '96, Verbik and Rook '97.

The rejection under 35 U.S.C . § 103(a) over Rook '96:

The examiner finds (Answer, page 8), "[c]laim 4 is directed to a method for treatment of advanced CTCL in [a] human with [an] effective amount of recombinant ... (IL-12) in a pharmaceutically acceptable carrier and an adjunct therapeutic agent stimulating ... (IFN-γ) production." According to the examiner (Answer, bridging paragraph, pages 8-9),

> it would have been obvious to the person of ordinary skill in the art at the time the invention was made to design a method as claimed for treatment of advanced CTCL in a human by administering recombinant IL-12 with an adjunct therapeutic agent stimulating IFN-γ (Th1 cytokine) production, based upon the strong teachings from Rook's in vitro [sic] studies and suggestions, that SzS, an advanced form of CTCL, is characterized with a marked depressed IFN- production, and a marked defect in IL-12 production by

> PBMCs, and that the presence of normal in vivo concentrations of both IL-12 and IFN-γ could favor the enhancement of anti-tumor cell-medicated immune responses that are deficient in this disorder. One of ordinary skill in the art would have been motivated to treat human CTCL by administering recombinant IL-12 with an adjunct therapeutic agent stimulating IFN-γ production at Rook's suggestion and reasonably would have expected success because such combination would correct both defects of IL-12 and IFN-γ in these patients, thus enhance anti-tumor immune responses.

In response appellant asserts (Brief, page 21), the cited prior art fails to provide a reasonable expectation of success in obtaining the claimed method. We agree. To establish a prima facie case of obviousness, there must be both some suggestion or motivation to modify the references or combine reference teachings and a reasonable expectation of success. In re Vaeck, 947 F.2d 488, 493, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991).

While we agree with the examiner that Rook '96 suggests a composition comprising a recombinant IL-12 in a pharmaceutically acceptable carrier together with an adjunct therapeutic agent that stimulates IFN-γ production, we disagree that Rook '96 provides a reasonable expectation of successfully treating advanced CTCL in a human. At best, Rook '96 suggests that controlled trials should be pursued (see Rook '96, page 316) to determine if such a composition would be effective in treating advanced CTCL. In our opinion, this is simply a suggestion to try -- "obvious to try," however, is not the standard of obviousness under 35 U.S.C. § 103. See In re O'Farrell, 858 F.2d 894, 903, 7 USPQ2d 1673, 1680 (Fed. Cir. 1988).

For the foregoing reasons, it is our opinion that the examiner fail to meet her burden of establishing a prima facie case of obviousness. Accordingly, we

reverse the rejection of claim 4 under 35 U.S.C. § 103(a) as being unpatentable over Rook '96.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED-IN-PART

Sherman D. Winters
Administrative Patent Judge

William F. Smith
Administrative Patent Judge

Donald E. Adams
Administrative Patent Judge

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